PET Scans Help Decisions In ER And Breast Cancer

A study has found 100% accuracy for subsequent outcomes with hormonal therapy

A small prospective study showed that PET imaging of the progesterone receptor (PgR) response to an estradiol challenge the usual predicted breast cancer response to hormonal therapy.

PET with a progestin-analog tracer showed increased PgR levels, indicative of functional estrogen receptors (ERs), in 28 postmenopausal women receiving endocrine therapy for metastatic or recurrent breast cancer, and all 28 benefited from treatment. In contrast, 15 patients without an increase in PgR levels did not benefit, representing 100% sensitivity and specificity. *Nature Communications* reported the 28 women with endocrine-responsive tumors lived significantly longer than did the women with nonresponsive tumors.

Farrokh Dehdashti, MD, of Washington University in St. Louis said the results suggest that PET imaging with the radiolabeled progestin-receptor analog could have a role in treatment selection and monitoring, said

“The fact that you can actually assess the [ER] function in the body was amazing,” she told MedPage Today. “It’s something that is very difficult to do. I’m really hopeful we can move to the next step and do a multicenter trial, if we can secure funding.”

For breast cancer, PET assessment of ER function should be applicable to all types of hormonal therapy. But the effects branch beyond just breast, Dehdashti says the strategy might also help guide therapeutic decision-making for other types of hormonally driven cancers.

Unfortunately, the 70%-80% of breast cancers are hormone-receptor (HR) positive, but as many as half of HR-positive tumors do not respond to endocrine therapy. Conventional testing for ER status of breast cancers is an imperfect predictor of tumor response to endocrine therapy, Dehdashti and colleagues noted.

Dehdashti and colleagues developed a PgR-binding progestin-analog radiotracer (21-[18F]fluoro furanyl norprogesterone, FFNP). In a preliminary evaluation, they observed significantly greater FFNP uptake in PgR-positive versus PgR-negative breast cancers with PET imaging. Their finding? A "rapid and robust" increase in FFNP uptake after estrogen treatment in a preclinical model of breast cancer, findings that were replicated in studies involving human breast cancer xenografts.

The accumulation of favorable experimental results led to a phase II evaluation of PET with FFNP in postmenopausal breast cancer. Investigators at Washington University's Siteman Cancer Center studied 43 women with locally advanced, locally recurrent, or metastatic HR-positive breast cancer scheduled to be treated with hormonal agents.

Hormonal treatment during the study included tamoxifen, aromatase inhibitors, fulvestrant, and gonadotropin-releasing hormone agonists, and most of them received a CDK4/6 inhibitor.

Baseline PET studies showed no difference in FFNP uptake prior (standardized uptake value, SUV) to estradiol challenge in the 28 patients who had stable disease or objective response to endocrine therapy and the 15 who did not benefit from treatment. Following the 1-day estradiol challenge, FFNP increased by an average of 25.4% in the 28 patients who subsequently benefited from treatment but decreased by 0.7% in the 15 women who did not benefit ($P<0.0001$). The percentage change in FFNP uptake did not vary significantly according to

prior therapy.

The 28 patients who benefited from hormonal therapy had at least a 7% increase in SUV for FFNP (responders), whereas none of the 15 nonresponding patients had as much as a 7% increase in SUV. The 7% threshold was associated with significantly longer overall survival (OS). After a median follow-up of 27.1 months, the estimated median OS was 22.6 months in patients who did not respond, but was not yet reached in responding patients ($P<0.0001$). Baseline FFNP uptake did not have a significant association with OS.

Ahead of the goal of a phase III trial in breast cancer, the study's author said the PET imaging strategy should interest oncologists who treat prostate cancer. Since androgen-receptor imaging agents already exist, so clinical interest by the genitourinary oncology community might provide impetus for more study.